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DOI: https://doi.org/10.1007/s00415-011-5922-3

Posted at the Zurich Open Repository and Archive, University of Zurich
ZORA URL: https://doi.org/10.5167/uzh-57530
Journal Article
Published Version

Originally published at:
Oberholzer, M; Poryazova, R; Bassetti, C L (2011). Sleepwalking in Parkinson's disease: a questionnaire-based survey. Journal of Neurology, 258(7):1261-1267.
DOI: https://doi.org/10.1007/s00415-011-5922-3

J Neurol (2011) 258:1261–1267
DOI 10.1007/s00415-011-5922-3

ORIGINAL COMMUNICATION

Sleepwalking in Parkinson's disease: a questionnaire-based survey

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Received: 6 July 2010 / Revised: 24 December 2010 / Accepted: 17 January 2011 / Published online: 4 February 2011
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Abstract Sleepwalking (SW) corresponds to a complex sleep-associated behavior that includes locomotion, mental confusion, and amnesia. SW is present in about 10% of children and 2–3% of adults. In a retrospective series of 165 patients with Parkinson's disease (PD), we found adult-onset ("de novo") SW "de novo" in six (4%) of them. The aim of this study was to assess prospectively and systematically the frequency and characteristics of SW in PD patients. A questionnaire including items on sleep quality, sleep disorders, and specifically also SW and REM sleep behavior disorder (RBD), PD characteristics and severity, was sent to the members of the national PD patients organization in Switzerland. In the study, 36/417 patients (9%) reported SW, of which 22 (5%) had adult-onset SW. Patients with SW had significantly longer disease duration ($p = 0.035$), they reported more often hallucinations ($p = 0.004$) and nightmares ($p = 0.003$), and they had higher scores, suggestive for RBD in a validated questionnaire ($p = 0.001$). Patients with SW were also sleepier (trend to a higher Epworth Sleepiness Scale score, $p = 0.055$). Our data suggest that SW in PD patients is (1) more common than in the general population, and (2) is associated with RBD, nightmares, and hallucinations. Further studies including polysomnographic recordings are needed to confirm the results of this questionnaire-based analysis, to understand the relationship between SW and other nighttime wandering behaviors in PD, and to clarify the underlying mechanisms.

Keywords Idiopathic Parkinson's disease · Sleepwalking · Nighttime wandering · REM sleep · Behavior disorder · Overlap parasomnia · Hallucinations

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Introduction

Sleepwalking (SW) corresponds to a complex sleep-associated behavior, usually initiated during arousals from slow-wave sleep, which includes locomotion, mental confusion, and amnesia regarding the episode. Injuries and acts of violence may also occur [1]. The prevalence of SW in children is about 10% and in adults is 2–3%. Less than 1% of adults reported never having walked in sleep in their childhood (adult-onset SW "de novo") [2]. Most commonly, SW appears in the context of a non-rapid eye movement (NREM) sleep parasomnia. However, SW can also appear in the context of nocturnal epilepsy, parasomnia overlap disorder, in which rapid eye movement (REM) and NREM features are combined, and psychiatric disorders [3]. SW is thought to arise from a dissociation between motor and mental arousal, as also suggested by a study using single-photon emission computed tomography [4]. Polysomnographic findings indicate an incomplete awakening that includes residual stage I theta patterns, some persistent slow-wave activity, and a diffuse and poorly reactive alpha rhythm [5]. In a patient with confusional arousals, which is an arousal parasomnia associated

with SW, Terzaghi et al. [6] succeeded in showing dissociated brain activity by intracerebral electroencephalography and evidenced these concurrently arising different states of being (i.e., wakefulness and NREM) as local brain phenomena.

An association of SW with Parkinson disease (PD) has been reported in an abstract form in three patients [7]. In two series of patients with REM sleep behavior disorder (RBD) and PD, one out of 100 consecutive patients and two of 66, respectively, had SW [8, 9]. We recently described SW in six out of 165 consecutive patients in a retrospective case series [10]. Sleepwalking/nighttime wandering has also been reported in ten of 93 Caucasian patients with RBD of different origin, including PD. Five of these ten patients had an underlying unspecified neurodegenerative disorder [11]. Night-wandering was also recently described in 11 of 70 Asian patients with RBD. Twenty-four had a symptomatic RBD, 11 of which had PD [12]. In questionnaire-based studies asking for sleepwalking/nighttime wandering in PD patients, frequencies ranging from 2% (4/201) [13], 3% (2/61, resp. 2/66) [9, 14] to 5% (16/303) [15] can be found in the literature, however, no detailed characteristics of the phenomenon were studied. The aim of the present study was to assess frequency and characteristics of SW/nighttime wandering in patients with PD.

Patients and methods

A questionnaire including items on sleep quality, sleep disorders, and specifically SW and RBD, PD characteristics, and severity, was sent to the members of the national PD patients organization in Switzerland. Members of the organization are not only PD patients but also their caregivers and relatives as well as many physicians. The questionnaire consists of 17 items on sleep and sleep disorders in general, including sleep duration, sleep-onset insomnia, sleep latency, sleep-maintenance insomnia, awakenings at night and their causes, early morning awakening, snoring, symptoms suggestive of sleep apnea, sleep talking, verbal and physical violence, restless legs symptoms, dream recall, variation of dream content, and nightmares and hallucinations. Possible answers include "yes" and "no" or provide a rating on a five-point scale depending on the frequency of occurrence ("almost always", "often", "occasionally", "seldom", or "never"). As a screening question for restless legs syndrome (RLS), the single validated question, suggested from the International RLS Study group was used [16]. All patients were asked if they had SW in childhood and/or as adults. The reported presence of SW was the main outcome measure of the study. The patients with SW filled in a more detailed questionnaire with 22 items on frequency of SW, occurrence during the night, recall, awakening during SW, most common and most complex activities, relation of SW behavior to dreams, injuries, violence, family history, precipitating factors.

Three validated scores were included in the questionnaire: the Epworth Sleepiness Scale (ESS) was used to assess subjective daytime sleepiness, the Activities of daily living (ADL) score according to Schwab and England was used as a marker of disease severity and the REM sleep behavior disorder screening questionnaire (RBDSQ) to assess RBD [17]. RBDSQ is a self-assessment tool consisting of ten items. Each question requires a "yes" or "no" answer. A cut-off score of five points was demonstrated to be suggestive of RBD—with a high sensitivity (96%) and specificity (92%) in idiopathic cases, but low specificity (56%) in cases with concomitant sleep disorders, especially in SW.

PD characteristics were addressed by six items gathering information on first symptoms, first diagnosis, and start of treatment, invasive treatment, and type of the PD. Furthermore, we asked patients to list their current medication. All patients also provided information and allowed us to contact their physicians if confirmation of the diagnosis was needed. Help from partners/caregivers was encouraged but was not mandatory. The study was approved by the local ethics committee and all patients signed an informed consent form (attached to the questionnaire).

Statistical analysis was performed using SPSS 15 software. Patients with SW were compared with patients without SW. Chi-square, t tests, and Mann–Whitney tests were used to analyze categorical and continuous variables, respectively. The significance level was set at $p < 0.05$. Missing cases were excluded analysis by analysis.

Results

A total of 417 questionnaires were returned. Characteristics of the study population are listed in Table 1. In 255 cases (61%), help from caregivers for filling in the questionnaire was reported.

Thirty-six (9%) out of 417 adult PD patients reported SW. Fourteen patients (3%) had SW since childhood, and in three of them it persisted throughout their lives. The remaining 22 patients (5%) had adult-onset SW, which appeared right before or after the diagnosis of PD onset.

The characteristics of patients with and without SW are presented in Table 2. Patients with SW showed a significantly longer disease duration (13.1 ± 9.0 vs. 10.3 ± 7.1; $p = 0.035$). However, no difference could be found comparing the ADL score (72 vs. 76%; $p = 0.25$).

Table 1 Demographic and clinical characteristics and treatment of the studied PD population ($n = 417$)

Variable	Mean ± SD or %, range	Missing cases, *n*
Age (years)	69.4 ± 9.1, 39–99	17
Gender	68% men	2
ESS	10.1 ± 5.3, 0–24	28
ESS ≥10	47	28
Sleep problem (%)	56.6	21
Disease duration (years)	10.5 ± 7.3, 0.5–54	32
ADL (%)	75.6 ± 16.7, 10–100	9
Help from caregivers[a]	255 (61%)	14
Therapy		[b]
Levodopa equivalent dose (mg)	686 ± 389, 0–2,869	
COMT inhibitors (%)	27	
Amantadine (%)	12	
Biperiden (%)	5	
MAO-B inhibitors (%)	12	
Antidepressants (%)	22	
Neuroleptics (%)	8	
Benzodiazepines[c] (%)	14	
Dementia medication (%)	3	

ESS Epworth Sleepiness Scale (score), *ADL* activities in daily life score according to Schwab and England

[a] Number of patients receiving help from their caregivers or bed partners to fill in the questionnaire

[b] Thirteen patients did not provide information on their therapy. Additionally, 36 patients did not provide the exact doses of the dopaminergic drugs

[c] Including imidazopyridines

Hallucinations ($p = 0.001$) and nightmares ($p = 0.006$) occurred more often in the sleepwalkers' group. In addition, they admitted their dream content and intensity to have changed recently, compared to the non-SW group ($p = 0.031$).

Patients with SW had significantly higher scores on the RBDSQ (6.8 ± 3.3 vs. 5 ± 3; $p = 0.001$). Twenty-six out of the 36 SW patients (72%) had scores ≥5, which is suggestive of RBD according to the literature [17].

There was a trend for higher ESS scores ($p = 0.055$) in patients with SW corresponding to a more pronounced excessive daytime sleepiness (EDS) (11.8 ± 5.7 vs. 10 ± 5.3).

When asked for the most complex action during SW, patients listed the following behaviors: preparing eggs for a meal, passing water in the corner of the room, fishing in the lake, climbing on furniture, shouting out of the window, trying to open the door of the apartment, framing pictures, opening the house door and climbing downstairs, taking down a painting from the wall, climbing over the bed railings and pacing around, singing, carrying towels and clothes out of the room, taking the window out of its frame, kicking the partner's legs. Several falls and jumps were mentioned as well.

The most common activities during SW are presented in Fig. 1.

Injuries during SW occurred in six (17%) out of 36 patients: bruises and contusions, bruises with wounds, hematoma on the thigh with residual dents, thumb and fingers injury, bleeding head injury, femoral neck fracture.

The most frequent factor that was reported to trigger SW was the full moon (11/36). Other triggers included "stress" (eight), alcohol (seven), pain (two), medications (two, once biperiden named, once zolpidem and pramipexole), "others" (two), and sleep deprivation (one).

No significant differences were found comparing results of questions asking for or suggesting other sleep disorders such as initiation and maintenance insomnia, snoring and sleep apnea, cursing and violence during sleep, restless legs, and dream recall.

Thirty-two (89%) patients received dopaminergic treatment. Out of these patients, 17 were treated with a combination of levodopa and a dopamine agonist, ten received a levodopa monotherapy, and five a dopamine agonist monotherapy. Other treatments included COMT inhibitors ($n = 8$), amantadine ($n = 5$, 14%), MAO-B inhibitors ($n = 6$, 17%), antidepressants ($n = 9$, 25%) including selective serotonin reuptake inhibitors (SSRIs, $n = 2$), serotonin-norepinephrine reuptake inhibitors (SNRIs, $n = 1$), tricyclics ($n = 5$) 5, mianserin ($n = 1$), neuroleptics ($n = 4$), rivastigmine ($n = 2$), and benzodiazepines ($n = 3$). There were no differences regarding the therapy (including neurosurgical treatment) between patients with and without SW except for a trend towards a slightly higher percentage of patients taking tricyclic antidepressants (14%) compared to the patients without SW (6%), $p = 0.072$.

Table 2 Characteristics of the patients with and without sleepwalking

Variable	Patients with SW, $n = 36$		Patients without SW, $n = 381$		p
	Mean ± SD, range	Missing cases, n	Mean ± SD, range	Missing cases, n	
Age (years)	70.2 ± 8, 55–88	1	69.4 ± 9, 36–99	16	NS
ESS	11.8 ± 5.7, 0–23	3	10 ± 5.3, 0–24	25	0.055
Disease duration (years)	13.1 ± 9, 3–48	3	10.3 ± 7.1, 0.5–54	29	0.035
Disease age (years)	57.1 ± 11.6, 27–78	3	58.9 ± 10.6, 27–88	29	NS
Levodopa equivalent dose (mg)	591 ± 325, 0–1,424	[a]	695 ± 393, 0–2,869	[b]	NS
ADL	72.4 ± 16.9, 30–90	1	75.8 ± 16.7, 10–100	8	NS
RBD score	6.8 ± 3.3, 1–13	1	5 ± 3, 1–13	12	0.001
Mean sleep duration (h)	6.9 ± 1.7, 3–9.5	0	6.4 ± 1.5, 2–11	20	NS
Sleep onset insomnia[c]	2.5 ± 1.3	2	2.4 ± 1.3	18	NS
Maintenance insomnia[c]	3.3 ± 1.4	2	3.4 ± 1.5	17	NS
Early morning awakening[c]	3.2 ± 1.3	0	3 ± 1.3	10	NS
Loud snoring[c]	2.6 ± 1.4	1	2.6 ± 1.1	23	NS
Apneas/hypopneas[c]	2.0 ± 1.3	3	1.6 ± 0.9	41	NS
Out of breath at night[c]	1.8 ± 0.9	0	1.5 ± 0.8	12	NS
Somniloquy[c]	2.8 ± 1.1	0	2.4 ± 1.1	11	NS
Cursing/violence[c]	1.6 ± 0.8	1	1.6 ± 1	17	NS
Restless legs symptoms[c]	2.4 ± 1.2	1	2.2 ± 1.3	13	NS
Nightmares[c]	2.5 ± 1.1	1	2 ± 0.9	10	0.006
Hallucinations[c]	2.3 ± 1.3	0	1.7 ± 1	9	0.001

ESS Epworth Sleepiness Scale (score), *ADL* activities in daily life score according to Schwab and England, *RBD* (REM sleep behavior disorder) score according to RBD Screening Questionnaire [17]

[a] Three patients did not provide information on their therapy and one did not provide the exact doses of the dopaminergic drugs

[b] Ten patients did not provide information on their therapy and 35 patients did not provide the exact doses of the dopaminergic drugs

[c] The frequency of the symptom is rated on a five-point scale (1, never; 2, seldom; 3, occasionally; 4, often; 5, almost always) and the p values represent the significance, based on Mann–Whitney nonparametric test

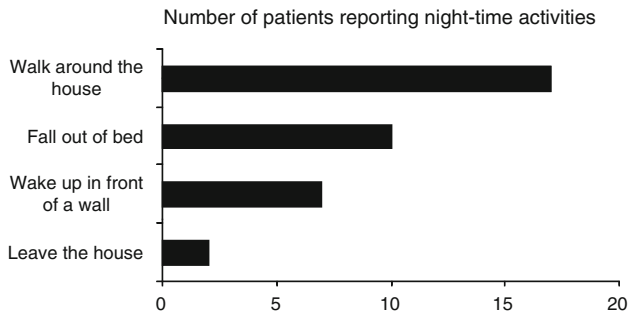

Fig. 1 Most common activities during SW

Discussion

Thirty-six (9%) out of 417 patients reported adult SW, and of them, 22 (5% of the population studied) reported adult-onset ("de novo") SW. Patients with SW had significantly longer disease duration; more hallucinations, nightmares, recent changes of their dream content; and higher scores in a validated questionnaire for REM sleep behavior disorder. Patients with SW also tended to be sleepier and to use tricyclic antidepressants more often.

Sleepwalking and Parkinson's disease: prevalence

Compared to the prevalence found in a large Finnish study [2], SW in patients with PD appears to be more frequent (9 vs. 2–4%). Comparing only adult-onset or "de novo" SW, we found a frequency considerably higher in the study population (5%) than in the general population (<1%).

It should, however, be stressed that our data were only based on information gathered by questionnaire. The differentiation of sleepwalking from other nighttime walking behavior (see below) is therefore not possible. Further studies including polysomnographic recordings and bed partner's reports are needed to elucidate the relationship between SW and other nighttime wandering behaviors in PD.

SW appears to be a late manifestation of PD. The longer disease duration suggests that neurodegenerative changes in advanced PD enable the clinical manifestation of SW. On the other hand, it did not correspond to the subjective grade of disability as expressed by the ADL score. One possible explanation of our finding could be that severe motor disability in PD patients prevents them from SW.

However, a significant motor improvement even in very disabled PD during REM sleep has been observed [8]. In one of our patients living in a nursery home, a dramatic improvement of locomotion during sleep as compared to wakefulness was similarly reported by his caregiver.

Sleepwalking and Parkinson's disease: association with hallucinations and cognitive decline

The significantly higher frequency of visual hallucinations in the SW group could just reflect a more advanced PD [18, 19]. The relation of VH with SW could arise, however, from similar neurodegenerative changes in brainstem and limbic structures [19]. Pathological changes in the amygdala correlate in fact with the occurrence of VH in PD [20, 21]; amygdala is on the other hand known to be involved in sleep-wake regulation and emotional control. Nocturnal agitation with VH resulting in the course of cognitive decline, as a third hypothesis, could mimic SW. Cognitive dysfunction is indeed common in PD, including impairment in executive functions and slowed information processing (bradyphrenia) [22, 23]. Nighttime wandering behaviors have been reported especially in male PD patients with severe cognitive decline living in nursing homes [24]. It is also typical for severe Alzheimer's disease [25]. Bliwise et al. [26] reported an even higher frequency of disruptive nocturnal behaviors in PD than in AD. This behavior (described as "sundowning phenomenon") appears predominantly in the evening hours when patients are still awake [27], while SW typically occurs hours after sleep onset. Whether SW in PD is linked to cognitive decline could unfortunately not be tested in our study.

Future studies in patients with neurodegenerative disorders should assess the relationship between SW, sundowning, and other nighttime wandering behaviors, and test the hypothesis that they all may belong to the clinical spectrum of the same underlying dysfunction of arousal/and motor control (see also Conclusions section).

Sleepwalking and Parkinson's disease: association with REM sleep behavior disorder

Patients with SW had higher scores in the RBDSQ. It was considered by its original authors that RBDSQ poorly discriminates patients with the most challenging differential diagnoses of RBD such as SW or epilepsy [17]. This could in fact explain the high RBDSQ scores in our patients. As a matter of fact, this questionnaire has never been validated in PD patients. The frequency of RBD in PD, as diagnosed by questionnaires, is different from video-polysomnographically diagnosed RBD (its frequency ranges from 33–47%), demonstrating the difficulty to predict RBD clinically [14, 28, 29]. It should be noted, however, that in a recent Japanese study, 54% of PD patients studied were diagnosed with RBD, based on questionnaire data [30]. If on one hand it is difficult to discriminate SW from RBD, based on questionnaire data, on the other hand the presence of one disorder does not necessarily exclude the other. For example, in our previous series of six patients with SW, four had RBD as well [10]. We postulate that a certain number of the PD patients suffer from both SW and RBD, a condition called "overlap parasomnia".

As discussed previously [10], this raises two pathophysiological explanations.

First, SW may represent an extreme, severe manifestation of motor dyscontrol in RBD and therefore belongs to the spectrum of this REM parasomnia. Getting out of bed and walking has been reported in a few series of patients with idiopathic and symptomatic RBD and was interpreted as a part of RBD motor activity [11, 12]. However, SW has not been documented with video-PSG to arise from REM sleep. In a detailed analysis of 100 consecutive patients with PD and a history of RBD, SW was observed in only one patient in whom RBD could not be demonstrated by video-PSG [8]. In addition, the characteristics of behavior in RBD and SW differ: RBD is usually described to be associated with short, jerky, rough and repetitive movements, although in 18% of the patients, not only violent movements are described but also gestures and complex movements, otherwise useless during sleep [31]. Furthermore, motor behaviors in our patients appear to be not only of a longer but also a more elaborate and physiological nature, similar to everyday activities (e.g., preparing a meal, fishing, climbing on furniture, framing pictures, etc.; see Results section above). Finally, although the combination of SW and RBD appears to be common in PD, not all of our patients had questionnaire results suggesting RBD, neither in the general section nor in the RBDSQ, thus suggesting that RBD is not mandatory for the appearance of de novo SW in patients with PD.

Second, the simultaneous occurrence of SW and RBD could suggest a common underlying disturbance of motor control during sleep in PD, with variable manifestations according to different sleep stages. This coexistence of SW and RBD during NREM and REM sleep, respectively, was named "overlap parasomnia", by Schenck et al. [32] in 33 patients. In that series, although an underlying disorder was found in a third of the patients, none had PD. Overlap parasomnia was rarely documented in the course of neurodegenerative diseases.

Sleepwalking and Parkinson's disease: other associations

Although conditions such as sleep apnea syndrome, RLS, or periodic limb movements in sleep have been shown to

trigger SW [33], we did not find significant differences regarding these symptoms.

Patients with SW also showed a trend towards a higher ESS. EDS in PD in general is multifactorial, in this case one possible explanation is sleep disruption due to SW, RBD, nightmares and hallucinations. EDS could also reflect a more advanced disease [34], in our case as expressed by longer disease duration in patients with SW.

Two of our patients claimed that biperiden had triggered SW episodes. Interestingly, one told that episodes ceased with stopping this anticholinergic treatment. Although neuro- and psychotropic medication has been described to induce confusional arousals and SW, especially lithium, longer acting benzodiazepines, and imidazopyridines as zolpidem and zopiclone [35, 36], our results did not show an association between SW and CNS-acting agents, including antiparkinsonian treatment. There was only a trend towards a higher consumption of tricyclics, but not for antidepressants in general.

Conclusions

As shown above, there is considerable evidence that SW in PD is more frequent than in the general population. The underlying pathophysiological mechanisms remain speculative. Various brainstem structures involved in locomotion, muscle tone regulation, and arousal as well as limbic and cortical areas are known to be affected in PD. Neurodegenerative changes at this level could affect the "ascending" control of state transition (leading to dissociated arousals from NREM and REM sleep) as well as the "descending" control of locomotion and muscle tone. Together these changes may lead to various sleep-associated behavioral disturbances, including SW (and more generally nighttime wandering behavior), RBD, and overlap parasomnia, as well as hallucinations and changes in dream generation.

Acknowledgments We thank Professor H.P. Ludin (Parkinson Centre, Humaine Clinic, Zihlschlacht, Switzerland) for his advice, and the national Parkinson's Disease patients organization in Switzerland (Parkinson Schweiz) for enabling us to send questionnaires to its members.

Conflict of interest The authors declare that they have no conflicts of interest. No study sponsorship or funding (industry, government, or institutional) was received.

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